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Statins Yes, Statins No: realities of Diabetic Dyslipidemia

Amid the significant number of “myths” or misconceptions regarding the management of LDL-C and its pharmacological treatment (always following the implementation of appropriate lifestyle and dietary measures) primarily with statins,

there is a wealth of diverse scientific evidence supporting the early and intensive management of this causal factor in atherosclerotic vascular disease. Below, we outline some realities that should help clarify the management of dyslipidemia in people with diabetes.

REALITY #1: LDL-C: THE ONLY CAUSAL (NOT ETIOLOGICAL) RISK FACTOR FOR ATHEROSCLEROTIC VASCULAR DISEASE (ASCVD). WHY IS IT STILL OVERLOOKED AND UNDERESTIMATED? (1)

Studies with various statins have shown that lower levels of LDL-C are associated with increased survival and a reduction in major adverse cardiovascular events (MACE). A meta-analysis including 10 studies with 79,494 patients demonstrated that statins reduce the incidence of coronary events, strokes, and overall mortality without affecting non-coronary mortality, benefiting both sexes regardless of the presence of diabetes, hypertension, and smoking (2).

A different meta-analysis of 27 randomized controlled clinical trials with 174,149 subjects showed that statins reduced the risk of major coronary events and coronary revascularization procedures by 24% and any stroke by 15% per 38mg/dL reduction in LDL-C (3).

Statins have become the cornerstone of LDL-C management (4). There is compelling evidence that best way to prevent ASCVD is to lower LDL-C in at-risk groups. Thirteen Nobel prizes have been awarded to scientists for their research on cholesterol. Our efforts should focus on educating and empowering physicians on the latest clinical practice guidelines, educating patients, and promoting shared decision-making. The benefits of clinical trials with statins and other lipid-lowering therapies can only be achieved if patients adhere to treatment and physicians are well-trained to provide appropriate treatment and counseling.

Our daily practice should aim for a common goal: achieving target LDL-C levels to prevent the onset of ASCVD.

REALITY #2: "RENOPROTECTIVE EFFECT"

Diabetes-related nephropathy is one of the leading causes of end-stage renal disease.

Recently, the therapeutic use of statins in patients with chronic kidney disease (CKD) was explored in a series of meta-analyses, revealing their potential to reduce mortality and cardiovascular complications in

this population, although not in patients undergoing hemodialysis. A study (5) reviews the current state of knowledge on the safety and efficacy profile of statins concerning renal outcomes in patients with diabetes and CKD. Evidence shows that statins may offer a beneficial renoprotective effect by inhibiting the progression of renal function deterioration. This effect is time-dependent and particularly strong in patients with type 2 diabetes mellitus and nephropathy.

REALITY #3: "MANAGEMENT OF DYSLIPIDEMIA IN CHILDREN WITH TYPE 1 DIABETES MELLITUS"

In recent decades, the risk of ASCVD has dramatically decreased among people affected by familial hypercholesterolemia (FH) due to early initiation of statin therapy in childhood. However, people with type 1 diabetes mellitus still have a 2 to 8 times higher risk of death vs the general population. Over the past 20 years, several landmark studies have been published on the excess mortality in people with type 1 diabetes mellitus, particularly young adults. Although these studies were conducted across different populations, they all reached the same conclusion: people with type 1 diabetes mellitus have a pronounced risk of ASCVD. Although type 1 diabetes mellitus and FH are different diseases, lessons could be learned from the early initiation of statins in children with FH, which may provide a rationale for stricter dyslipidemia control in children with type 1 diabetes mellitus (6).

REALITY #4: "WE SHOULD LOOK AT THE NUMBER AND QUALITY OF LIPID PARTICLES. RESIDUAL RISK"

There is little information on the relationships between serum levels of small dense low-density lipoproteins (sdLDL-C) and serum triglycerides (TG) and cardiovascular events in patients with coronary artery disease (CAD) and type 2 diabetes mellitus (T2DM) on statins. The aim of this study was to evaluate the relationships between serum TG levels and sdLDL-C levels as residual risks for cardiovascular events in patients with coronary artery disease and T2DM on statins. »

STATINS CAN OFFER A BENEFICIAL RENOPROTECTIVE EFFECT BY INHIBITING THE PROGRESSION OF RENAL FUNCTION DETERIORATION. THIS EFFECT IS TIME-DEPENDENT AND IS PARTICULARLY STRONG IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND NEPHROPATHY

THERE IS
COMPELLING
EVIDENCE THAT
THE BEST WAY
TO PREVENT ASCVD
IS BY REDUCING
LDL-C LEVELS
IN AT-RISK GROUPS



» Results:

The incidence of cardiovascular events was significantly higher in patients with sdLDL-C \geq 40.0 mg/dL and TG $<$ 150 mg/dL, as well as in patients with sdLDL-C \geq 40.0 mg/dL and TG \geq 150 mg/dL, but not in patients with sdLDL-C $<$ 40.0 mg/dL and TG \geq 150 mg/dL vs patients with sdLDL-C $<$ 40.0 mg/dL and TG $<$ 150 mg/dL.

Conclusions:

Under statin therapy, patients with CAD and T2DM who had sdLDL-C levels \geq 40.0 mg/dL were at high risk of cardiovascular events even if serum TG levels were controlled at $<$ 150 mg/dL. Diabetes mellitus (DM) is an established risk factor for ASCVD (atherosclerotic cardiovascular disease): 1). ASCVD-related cardiovascular events are the main cause of morbidity and mortality in patients with T2DM. It has been shown that patients with a combination of T2DM plus a history of cardiovascular disease have a very high risk for new cardiovascular events.

Therefore, the American Diabetes Association (ADA) recommends high-intensity statin therapy in patients with ASCVD and T2DM. Statin therapy has been shown to reduce the risk of cardiovascular events in patients with CAD by about 20%. However, residual cardiovascular risks remain in patients on statins. Elevated serum TG levels are known to contribute to residual cardiovascular event risks. The level for considering hypertriglyceridemia according to the clinical practice guidelines is 150 mg/dL, and these serum TG levels are elevated in most patients with T2DM, predicting cardiovascular disease. Several studies have shown that a high level of small, dense low-density lipo-

protein cholesterol (sdLDL-C) also produces a residual cardiovascular risk in patients on statins.

sdLDL particles are defined as those with a diameter of \leq 25.5 nm and a density of 1.044 to 1.063 g/mL. In patients with T2DM, serum LDL-C does not generally increase markedly, but serum sdLDL-C and TG levels do. **D**

CONCLUSIONS:

- Some aspects have been summarized that may create controversy when discussing dyslipidemia and its management.
- We have also detailed much of the available evidence to provide clarity and assertiveness when it comes to minimizing the risk of an atherosclerotic vascular event related to elevated LDL-C levels.
- This is intended to serve as a guide for readers who wish to delve deeper into this fascinating area of lipidology.

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